THE WALTER & ELIZA HALL INSTITUTE OF MEDICAL RESEARCH

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Director:
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Professor Joshua Lederberg,
Dept. of Genetics,
Stanford University School of Medicine,
PALO ALTO, CALIFORNIA.

Dear Josh,

Thank you very much for your note and enclosures. I have passed the invoices dealing with the microscope on to Mr. Hughes, and no doubt you have received a cheque by now. Might I say once again how grateful I am to you for saving our lives in this regard. We all heaved a deep sigh of relief when the microscope came.

Unfortunately the two excellent references to the chaining phenomenon arrived a little bit too late for inclusion in my Stanford papers, but they certainly will come in handy later on. Thank you very much for that too.

I was very excited to see that you have moved seriously into the area of mental retardation, though I am a little skeptical about the experimental approach which you have outlined. I realize that this type of Captain Cook work has to be done sometime, but I doubt whether the country chartered would be as fertile as Australia, even. But as you suggest, it is getting the right sort of people interested in the area, and getting some work going along these lines that is the important thing. It matters little whether the research project one year after its start has already deviated along the way from the line indicated.

I am now fairly certain about my dates in America in June. On present plans, I'll be arriving in San Francisco on the evening of June 6th, and will be staying in the Bay area till the evening of 11th or the morning of the 12th. The temptation to see all of you again when the Paris invitation came proved too much for me. I was delighted to hear that you will be back from Japan by that time.

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You will be interested to hear that we now find that the precursor of plasma cells in a primary response to bacterial antigens is also a primitive lymphocyte, in fact the primary response seems to be merely a scaled down version of the secondary response. The crucial difference in cellular proliferation between the primary and the secondary responses appears to be a maturation arrest of the blast cells between the second and the fourth day after antigen injection. In the secondary response, the cells started differentiating into plasma blasts and plasma cells virtually from time zero, whereas in the primary response, they appear to start multiplying almost without lag, but remain quite primitive for the first 3 days, and the first sign of antibody production by single cells is on the 4th day. If one extrapolates the proliferation curves back to the time of antigen injection, one gets the impression that too many cells are proliferating and eventually differentiating for any straight forward clonal selection approach. I know that unknown questions of nett emigration of cells into the node are a qualifying factor here. On the other hand, we are thinking more and more along the lines of the primitive lymphocyte as a "mother" or "nurse" cell rather than as a "memory" cell. The possibility that the information is being transmitted from another cell type is still prominent in our minds.

Before these alternatives can be tackled experimentally, we need a tremendous amount of background information about the behaviour of RNA in antibody forming cells and their ancestors, which with the collaboration of Gordon Ada we are just beginning to get. Eventually direct transfers of RNA derived from a cell with one competence into another cell with another or no competence should be possible.

Please give our fondest love to Esther. Lyn won't be able to make it with me this time, but is already agitating very actively for another swing around the world in 1964. We'll see!

As ever,

GUS.